the corresponding areas of the stimulable phosphor sheet can absorb and store radiation energy of the radioactive label coming from the DNA fragments fixed to the DNA micro-array;

irradiating the radiation image storage panel with a stimulating light, so that the image storage panel releases a stimulated emission from the area in which the radiation energy is stored;

detecting the stimulated emission photoelectrically to obtain a series of electric signals; and

processing the electric signals to locate the area in which the complementary DNA fragments are fixed.

REMARKS

STATUS OF THE CLAIMS

Claims 1-3, 6 and 7 are pending in the present application.

REJECTION OF CLAIMS 1-3 UNDER 35 U.S.C. 112; REJECTION OF CLAIMS 1-3 UNDER 35 U.S.C. 102(e)

Applicants gratefully acknowledge that the rejections of the claims under 35 U.S.C. 112, second paragraph, and under 35 U.S.C. 102(e) over U.S. Patent 6,256,405 to Some et al. have been withdrawn by the Examiner.

REJECTION OF CLAIMS 1-3 AND 6-7 UNDER 35 U.S.C. 103(a)

Claims 1-3 and 6-7 have been rejected by the Examiner under 35 U.S.C. 103(a) over U.S. Patent 6,256,405 to Some et al. in view of U.S. Patent 6,271,002B1 to Linsley et al. in view of U.S. Patent 4,711,955 to Ward et al. for the reasons set forth in paragraphs 2-5 of the Office Action. These rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Present Invention

A first embodiment of the present invention as recited in claim 1, as amended, relates to a process for detecting a complementary DNA fragment which comprises the steps of bringing single-stranded sample DNA fragments having a radioactive label in a liquid phase into contact with a DNA micro-array having a support and at least two defined areas in each of which a group of probe compounds selected from the group consisting of DNA molecules, DNA fragments, synthesized oligonucleotides, synthesized polynucleotides, and PNA are fixed under such condition that a group of the probe compounds fixed in one area differs from a group of the probe compounds fixed in another area, so that DNA fragments complementary to a group of the probe compounds are fixed by hybridization to the area in which the last-mentioned group is fixed; removing unfixed sample DNA fragments from the DNA micro-array; keeping the DNA micro-array

in contact with a radiation image storage panel which has divided stimulable phosphor layers containing a stimulable phosphor in areas corresponding to the areas on which groups of the probe compounds are fixed, so that the corresponding areas of the stimulable phosphor sheet can absorb and store radiation energy of the radioactive label coming from the DNA fragments fixed to the DNA micro-array; irradiating the radiation image storage panel with a stimulating light, so that the image storage panel releases a stimulated emission from the area in which the radiation energy is stored; detecting the stimulated emission photoelectrically to obtain a series of electric signals; and processing the electric signals to locate the area in which the complementary DNA fragments are fixed.

A second embodiment of the present invention as recited in claim 6, as amended, relates to a process for detecting a complementary DNA fragment which comprises the steps of bringing single-stranded sample DNA fragments having a radioactive label in a liquid phase into contact with a gridded DNA micro-array on a solid support having at least two defined areas in each of which a group of probe compounds selected from the group consisting of DNA molecules, DNA fragments, synthesized oligonucleotides, synthesized polynucleotides, and PNA are fixed under such condition that a group of the probe compounds fixed in one area differs from a group of the probe compounds fixed in another area, so that DNA fragments complementary to a group of the probe compounds are fixed by hybridization to the area in

which the probe compounds are fixed; removing unfixed sample DNA fragments from the DNA micro-array; keeping the DNA micro-array in contact with a radiation image storage panel which has divided stimulable phosphor layers containing a stimulable phosphor in areas corresponding to the areas on which groups of the probe compounds are fixed, so that the corresponding areas of the stimulable phosphor sheet can absorb and store radiation energy of the radioactive label coming from the DNA fragments fixed to the DNA micro-array; irradiating the radiation image storage panel with a stimulating light, so that the image storage panel releases a stimulated emission from the area in which the radiation energy is stored; detecting the stimulated emission photoelectrically to obtain a series of electric signals; and processing the electric signals to locate the area in which the complementary DNA fragments are fixed.

Clarification of the Present Invention

The characteristic feature of the present invention relates to the construction of the radiation image storage panel employed in the claimed process, as follows:

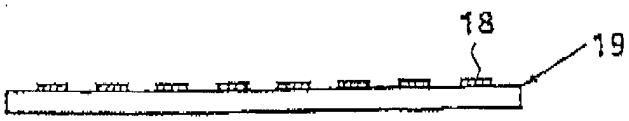
> "keeping…radiation image storage panel which has divided stimulable phosphor layers containing a stimulable phosphor in areas corresponding to the areas on which groups of the probe compounds are fixed, so that the corresponding areas of the stimulable phosphor sheet can absorb and store radiation energy of the radioactive label coming from the DNA fragments fixed to the DNA micro-array"

A representative configuration of the claimed radiation image storage panel of the invention is illustrated in Figs. 1-3 in which the phosphor layers are divided on the support. This corresponds to the "discontinuous stimulable phosphor layer" described in the specification at page 6, lines 25-27, which recites:

> In Fig. 3, the radiation image storage panel 19 is composed of a support sheet and a discontinuous stimulable phosphor layer 18...

Figure 3 is shown below for the Examiner's convenience:

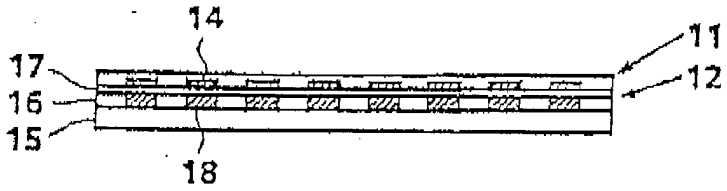
FIG. 3



The divided phosphor layers are arranged in the positions corresponding to the areas of the micro-array sheet so as to efficiently absorb radiation emitted from the radioactively labeled sample DNA fragments attached to the probe compounds fixed to the corresponding positions of the micro-array sheet only, as shown in Figs. 2 and 3 of the present specification.

Figure 2 is shown below for the Examiner's convenience:

FIG. 2



Accordingly, in order to more clearly define the present invention, the phrase in claim 1, line 17 and in claim 6, line 17 which reads: "radiation image storage panel containing..." has been amended to read: --radiation image storage panel which has divided stimulable phosphor layers containing--. The phrase "the area of stimulable phosphor" at claim 2, lines 2-3 has been amended to recite --areas of stimulable phosphor layers."

The radiation image storage panel having the claimed configuration including the above-mentioned divided or discontinuous phosphor layers, such as that illustrated in Fig. 2, are "almost free from noises [sic] caused by the inadvertently fixed non-complementary DNA fragments". See the specification at page 3, lines 3-8, which recites the following:

The present invention provides an improved method for detecting complementary DNA fragments utilizing a combination of the conventional DNA micro-array and the conventional radiation image storage panel, which is almost free from noises caused by the inadvertently fixed non-complementary DNA fragments.

Details of the "noises" are discussed on page 2, lines 26-35 of the specification as follows:

According to the studies performed by the present inventors, however, the high sensitivity of the radiation image storage panel sometimes shows analytical errors which are caused by the fact that the high sensitive radiation image storage panel absorbs not only the radiation energy emitted by the target DNA fragments (that is, the complementary DNA fragments but also radiation energy emitted by the non-target DNA fragments (that is, non-complementary DNA fragments) which are inadvertently fixed to the DNA micro-array not by hybridization.

The Some et al. Reference

Figures 1 and 8 of the Some et al. reference as shown below for the Examiner's convenience:

FIG. 1

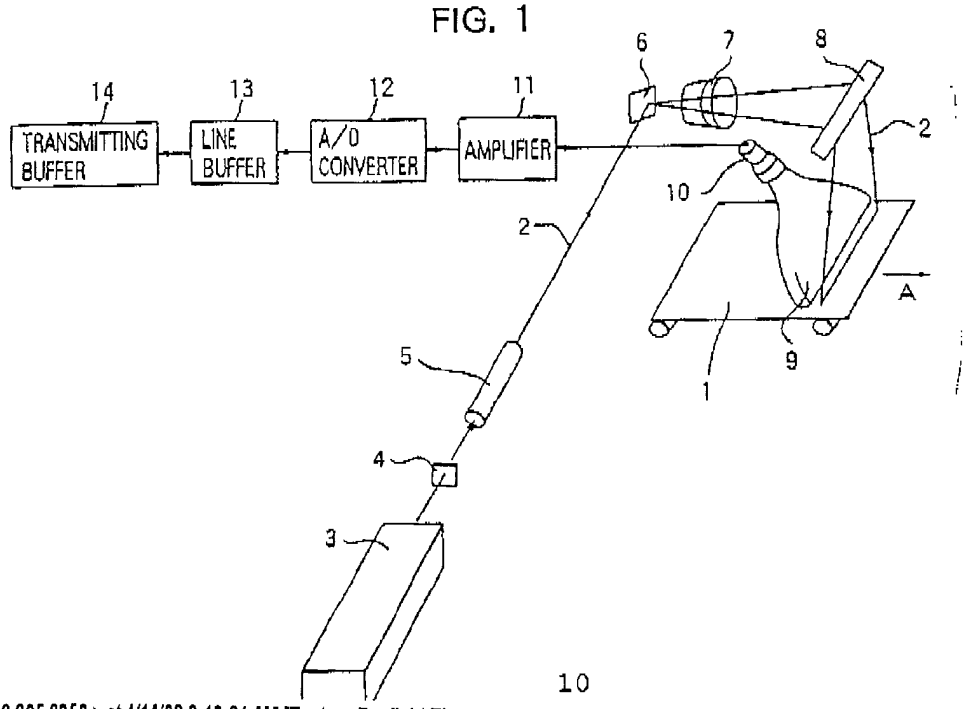
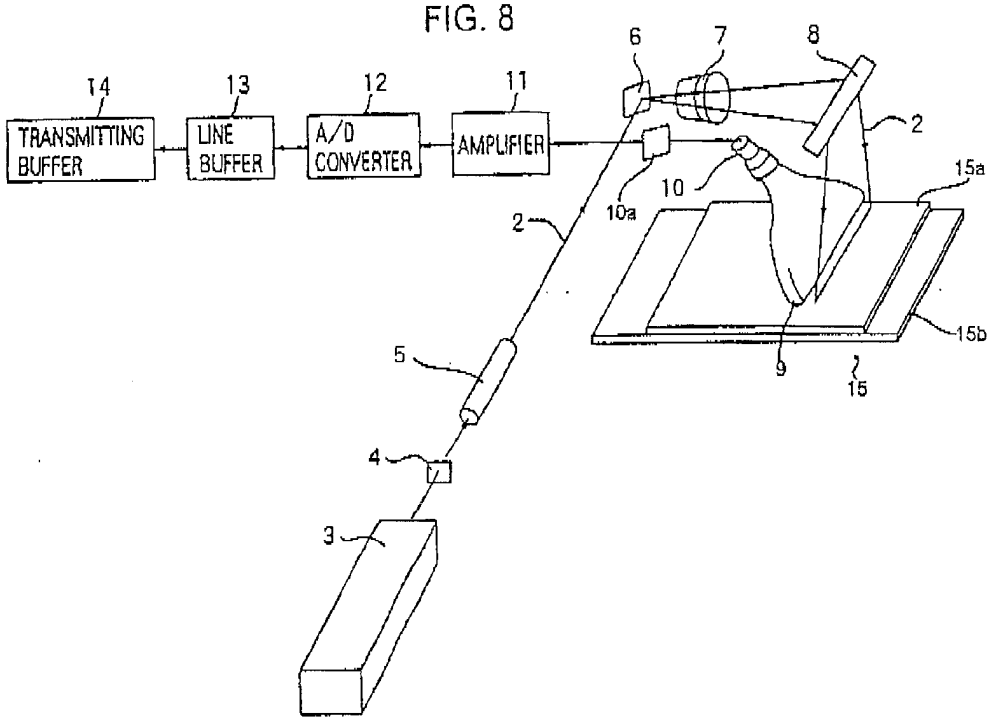


FIG. 8



The Some et al. reference utilizes an undivided sample sheet.

U.S. Patent 6,271,002B1 to Linsley et al.

As indicated in the Abstract of the Disclosure of the Linsley et al. reference, the invention relates to methods and kits for amplification of mRNA using a primer in PCR that contains an RNA polymerase promoter. The invention provides methods for amplification and detection of RNA.

U.S. Patent 4,711,955 to Ward et al.

The Ward et al. patent teaches compounds having certain structures as shown in the Abstract thereof.

Distinctions Between the Present Invention and the Cited Prior Art

Contrary to the present invention, the radiation image storage panel 1 and 15 as shown in Figs 1 and 8 of the Some et al. reference is an individual sample sheet. There is no suggestion or disclosure of divided stimulable phosphor layers in the sheet of the Some et al. reference.

The Examiner's attention is further directed to col. 7, lines 43-50 of the Some et al. reference, which recites the following:

> The thus obtained transfer support and the stimulable phosphor sheet 1 are placed in layers for a certain period of time to expose the stimulable phosphor sheet 1 and at least a part of radiation emitted from the radioactively labeled substance on the transfer support is absorbed in the stimulable phosphor sheet 1, whereby the locational information regarding the radioactively labeled substance in the specimen is stored in the stimulable phosphor sheet 1.

The Examiner states on page 3 of the Office Action that "Some et al. teach a process for detecting a complementary DNA fragment which comprises the steps of:..."

> "C) keeping the hybridized DNA in contact with a radiation image storage panel containing a stimulable phosphor in areas corresponding to the areas on which groups of DNAs are hybridized, so that the corresponding areas of the stimulable phosphor sheet can absorb and store radiation energy of the radioactive label coming from the fixed DNA fragments through the openings (Figures 1 and 8 and Column 7, lines 43-50);"

The above quotation highlights the Examiner's misunderstanding of the present invention vis-à-vis the prior art. Each of the Some et al. Figs. 1 and 8 show a radiation image storage panel with a sample sheet. See ref. Num. 1 of Fig. 1 and ref. Num. 15 of Fig. 8. The Examiner should further note that there are no dotted stimulable phosphor layers illustrated in the cited prior art.

The Examiner should especially note that the phrase "at least a part of radiation is absorbed in the stimulable phosphor sheet" means "some of radiation advances not towards the stimulable phosphor sheet and therefore is not absorbed in the stimulable phosphor sheet".

Accordingly, the cited Some et al. reference is completely silent with respect to the characteristic feature of the claimed process utilizing the claimed radiation image storage panel.

With respect to the Linsley et al. patent, the Examiner relies upon the description at col. 23, line 50 to col. 27, line 24. However, this disclosure merely teaches that "microarrays are known in the art". See col. 23, line 51.

The Examiner's motivation for combining the teachings of Some et al and Linsley et al. is that "By employing scientific reasoning, an ordinary artisan would have combined...[the references]". However, the Examiner can not and does not refer to any portion of either the Some et al. reference or the Linsley et al. reference to provide the necessary motivation for combining the teachings thereof in order to obtain the present invention.

The necessary motivation for the combination must come from the prior art. The fact that references can be combined or modified is not sufficient to establish *prima facie* obviousness. See MPEP 2143.01.

Accordingly, since the two isolated disclosures are taught somewhere in the art, the Examiner basically states that because the individual components of the invention exist, then it would be obvious to combine the disclosures in order to obtain the present invention. However, this "obvious to try" rationale has been repeatedly rebuked by the courts. The Examiner is using the present specification as a roadmap in order to combine random teachings of the prior art in an attempt to obtain the present invention. Such improper hindsight does not establish a prima facie case of obviousness. See MPEP 2145XB.

Indeed, not only does the combination of Some et al. and Linsley et al. fail to provide motivation to combine the teachings thereof, the combination fails to even teach the present invention. The Examiner's reliance on the Ward et al. reference does not correct the deficiencies of the combination of references.

None of the references relied by the Examiner when taken together, disclose or suggest the use of radiation image storage panel employed in the claimed process, as follows:

> "keeping...radiation image storage panel which has divided stimulable phosphor layers containing a stimulable phosphor in areas corresponding to the areas on which groups of the probe compounds are fixed, so that the corresponding areas of the stimulable phosphor sheet can absorb and store radiation energy of the radioactive label coming from the DNA fragments fixed to the DNA micro-array"

The Examiner's motivation for combining the teachings of the Ward et al., Some et al and Linsley et al. on page 6 of the Office Action is that "By employing scientific reasoning, an ordinary artisan would have combined...[the references]". The Examiner relies upon the teaching at col. 3, lines 11-17 of the Ward et al. reference to provide the necessary motivation to combine the teachings of the Ward et al. references with the remaining references:

> Moreover, these nucleotide derivatives are chemically stable and can be expected to have functional shelf-lives of several years or more. Finally, these compounds permit the development of safer, more economical, more rapid, and more reproducible research and diagnostic procedures.

The above cited quote basically says "try our compounds", making the Examiner's motivation for the combination the discredited "obvious to try" type rejection.

Just as importantly, modifying the teachings of either the Linsley et al. or Some et al. references in the manner suggested by the Examiner would destroy the teachings of these references. See In re Gordon, 221 USPQ 1125 (Fed. Cir. 1984). For instance, modifying the Linsley et al. reference in the manner suggested by the Examiner would destroy the primary teachings of the Linsley

et al. reference.

In summary, the secondary prior art references, namely, Linsley et al. and Ward et al. are completely silent with respect to the above-mentioned characteristic feature of the present invention (e.g. process using claimed radiation storage panel). Therefore, the Examiner has not established a *prima facie* case of obviousness since the prior art does not disclose or suggest all of the claimed limitations. Accordingly, the claimed invention is not obvious over the teachings of the cited prior art references.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three month extension of time for filing a response in connection with the present application. The required fee of $920.00 is being submitted with the Notice of Appeal filed concurrently herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Claims 1, 2 and 6 have been amended as follows:

Claim 1 (Twice Amended) A process for detecting a complementary DNA fragment which comprises the steps of:

bringing single-stranded sample DNA fragments having a radioactive label in a liquid phase into contact with a DNA micro-array having a support and at least two defined areas in each of which a group of probe compounds selected from the group consisting of DNA molecules, DNA fragments, synthesized oligonucleotides, synthesized polynucleotides, and PNA are fixed under such condition that a group of the probe compounds fixed in one area differs from a group of the probe compounds fixed in another area, so that DNA fragments complementary to a group of the probe compounds are fixed by hybridization to the area in which the last-mentioned group is fixed;

removing unfixed sample DNA fragments from the DNA micro-array;

keeping the DNA micro-array in contact with a radiation image storage panel which has divided stimulable phosphor layers containing a stimulable phosphor in areas corresponding to the areas on which groups of the probe compounds are fixed, so that the corresponding areas of the stimulable phosphor sheet can absorb and store radiation energy of the radioactive label coming from the DNA fragments fixed to the DNA micro-array;

irradiating the radiation image storage panel with a

stimulating light, so that the image storage panel releases a stimulated emission from the area in which the radiation energy is stored;

detecting the stimulated emission photoelectrically to obtain a series of electric signals; and

processing the electric signals to locate the area in which the complementary DNA fragments are fixed.

Claim 2 (Twice Amended) The process of claim 1, in which area on the radiation image storage panel other than the [area] areas of stimulable phosphor layers is covered by a physical barrier member made of non-radiation transmitting material selected from the group consisting of metal, ceramic material, and polymer material.

Claim 6 (Amended) A process for detecting a complementary DNA fragment which comprises the steps of:

bringing single-stranded sample DNA fragments having a radioactive label in a liquid phase into contact with a gridded DNA micro-array on a solid support having at least two defined areas in each of which a group of probe compounds selected from the group consisting of DNA molecules, DNA fragments, synthesized oligonucleotides, synthesized polynucleotides, and PNA are fixed under such condition that a group of the probe compounds fixed in one area differs from a group of the probe compounds fixed in another area, so that DNA fragments complementary to a group of

the probe compounds are fixed by hybridization to the area in which the probe compounds are fixed;

removing unfixed sample DNA fragments from the DNA micro-array;

keeping the DNA micro-array in contact with a radiation image storage panel which has divided stimulable phosphor layers containing a stimulable phosphor in areas corresponding to the areas on which groups of the probe compounds are fixed, so that the corresponding areas of the stimulable phosphor sheet can absorb and store radiation energy of the radioactive label coming from the DNA fragments fixed to the DNA micro-array;

irradiating the radiation image storage panel with a stimulating light, so that the image storage panel releases a stimulated emission from the area in which the radiation energy is stored;

detecting the stimulated emission photoelectrically to obtain a series of electric signals; and

processing the electric signals to locate the area in which the complementary DNA fragments are fixed.